

## REMARKS

Claims 1-3, 8, 10, and 11 have been amended. Claims 9, 12-43, and 45-54 have been canceled without prejudice or disclaimer. Claims 1-8, 10, 11, and 44 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 10, line 9; page 14, line 16; page 17, line 1; in Figures 1A-1B, and in the Sequence Listing. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

### **1. Claim of priority**

The Office Action asserts that because the nucleotide sequence of SEQ ID NO: 1, the DNA insert in ATCC Deposit No. PTA-1882, and the limitation “at least about 70 percent identical to the polypeptide as set forth in SEQ ID NO: 2” are not disclosed in U.S. Provisional Application No. 60/188,786 (the ‘786 application), from which the instant application claims priority, in the manner provided by 35 U.S.C. § 112, first paragraph, these limitations are not entitled to the benefit of the filing date of the ‘786 application under 35 U.S.C. § 119(e). The Action states that the subject matter recited in claims 1, 2, 4-8, 10, 11, and 44 is therefore entitled only to the March 13, 2001 filing date of instant application. Applicants respectfully contend that only the initial priority determination (*i.e.*, that the nucleotide sequence of SEQ ID NO: 1 is not entitled to the benefit of the March 13, 2000 filing date of the ‘786 application) is relevant to the rejections made in the instant Action (*see* discussion in sections 3 and 5 below), and therefore, that only this determination must be addressed.

As shown in Exhibit A, the nucleotide sequence disclosed in Figure 1 of the ‘786 application is 100% identical to nucleotide residues 610 through 1242 of the nucleotide sequence set forth in SEQ ID NO: 1. However, because the FGF-L open reading frame also comprises nucleotide residues 610 through 1242 of the nucleotide sequence set forth in SEQ ID NO: 1, residues 1 through 609 merely constitute the 5’ untranslated portion of the FGF-L cDNA sequence and residues 1246 through 1330 merely constitute the 3’ untranslated portion of the FGF-L cDNA sequence (residues 1243 through 1245 constituting the stop codon). Applicants respectfully contend that the portion of the nucleotide sequence of SEQ ID NO: 1 that encodes FGF-L polypeptide (*i.e.*, the amino acid

sequence set forth in SEQ ID NO: 2) is disclosed in U.S. Provisional Application No. 60/188,786 (the '786 application) in the manner provided by 35 U.S.C. § 112, first paragraph, and therefore, that this sequence is entitled to the benefit of the filing date of the '786 application under 35 U.S.C. § 119(e).

**2. Rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 101**

The Office Action asserts a rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 101. The Action states that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The Action also states that, in view of Galzie *et al.*, 1997, *Biochem. Cell Biol.* 75:669-85, which discloses that the FGF family of proteins encompasses a group of polypeptide mitogens eliciting a wide variety of responses, and Koga *et al.*, 1999, *Biochem. Biophys. Res. Commun.* 261:756-65, which discloses that the expression pattern of FGF-20 and FGF-9 differs, the members of the FGF family of proteins lack a common utility applicable to all members of this family. The Action further states that one of ordinary in the art would not accept mere homology as establishing a function of a protein. Applicants traverse this rejection.

Applicants contend that the specification contains an assertion of a specific and substantial utility for the claimed invention that would be credible to one of ordinary skill in the art. The instant specification teaches a human cDNA of 1330 nucleotides encoding an FGF-L polypeptide of 211 amino acids (Figures 1A-1B). The instant application also teaches that FGF-L polypeptides share a high degree of sequence similarity with the members of the FGF family of proteins, and the highest degree of sequence identity with FGF-9 and FGF-16 (Figures 2-4 and page 74, lines 18-19). A ClustalW sequence alignment of the amino acid sequences of FGF-9 or FGF-16 and human FGF-L polypeptide clearly illustrates the close structural relationship between FGF-L polypeptide and FGF-9 and FGF-16 (*see* Exhibit B); the former sequence sharing 68% sequence identity (and 80% similarity) with FGF-L polypeptide and the latter sequence sharing 62% sequence identity (and 82% similarity) with FGF-L polypeptide. This close relationship is further illustrated in the guide tree shown in Exhibit C (the sequence alignment and guide tree shown in Exhibits B and C were prepared using the application MacVector 7.1.1; Accelrys; Cambridge, UK, at the default settings and amino acid sequences that were publicly available at the time the instant application was filed). In addition, nearly all of the related amino acid sequences identified in a BLAST search using the human FGF-L

amino acid sequence (SEQ ID NO: 2) are members of the FGF family of proteins (*see* Exhibit D; sequences that were publicly available at the time the instant application was filed are indicated in bold). Applicants contend that such sequence analyses could be performed at the time the instant application was filed using the teachings in the instant application and knowledge in the art by one having but ordinary skill in the art.

Applicants also note that the human FGF-L polypeptide disclosed in the instant application shares substantial amino acid sequence similarity with the *Xenopus* FGF molecule, XFGE-20, disclosed by Koga *et al.*, 1999, *Biochem. Biophys. Res. Commun.* 261:756-65 (*see* Exhibit E, which was prepared using the application MacVector 7.1.1 at the default settings). Koga *et al.* disclose that XFGE-20 is expressed in *Xenopus* embryos during the blastula stage and in the stomachs and testis of adults. Applicants contend that one of ordinary skill in the art, at the time the application was filed, would have recognized that the human FGF-L polypeptide disclosed in the instant application, which shares 80% sequence identity and 89% sequence similarity with human FGF-L polypeptide, is, in fact, the human ortholog of XFGE-20.

Applicants contend that based on the totality of the evidence of record, one of ordinary skill in the art would recognize that FGF-L: polypeptide is a member of the FGF family of proteins – namely, FGF-20. In fact, the results of the BLAST search described above indicate that those of ordinary skill in the art, absent Applicants’ teaching, *have* recognized that the human polypeptide set forth in SEQ ID NO: 2 is a member of the FGF family of proteins (*i.e.*, FGF-20), albeit subsequent to Applicants’ identification of this member of the FGF family (*see* Kirikoshi *et al.*, GenBank Accession Nos. BAB03633, published August 2, 2000, JC7353, published December 1, 2000, and Q9NP95, published October 16, 2001; Omachi *et al.*, GenBank Accession No. BAB03530, published November 11, 2000; and Jeffers *et al.*, GenBank Accession No. NP\_062825, published April 6, 2003). Moreover, as members of the FGF family have substantial real world use, for example, as regulators of cell proliferation, differentiation, and function (Galzie *et al.*, 1997, *Biochem. Cell Biol.* 75:669-85), and the teachings of Koga *et al.* indicate that FGF-20 plays a role in cell differentiation at the blastula stage of development,, Applicants contend that one of ordinary skill in the art would recognize that the claimed molecules have credible, specific, and substantial utility.

Applicants contend that because the instant application contains an assertion of a specific and

substantial utility for the claimed invention credible to one of ordinary skill in the art, the rejection under 35 U.S.C. § 101 should be withdrawn.

**3. Rejections of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 112, first paragraph**

The Office Action asserts a rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that because the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention.

Applicants have set forth above affirmative evidence that the asserted utility would be credible to one of ordinary skill in the art. Applicants contend that because the instant application contains an assertion of a specific and substantial utility for the claimed invention that one of ordinary skill in the art would find to be credible, this rejection should be withdrawn.

The Office Action also asserts a rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that because ATCC Deposit No. PTA-1882 does not appear to be publicly available or capable of being reproducibly isolated from nature without undue experimentation, and the claims require the use of this deposit, the mere reference to the deposit in the specification is insufficient to ensure that all of the conditions of 37 C.F.R. §§ 1.803-1.809 have been met. The Action also states that a deposit made in full compliance with 37 C.F.R. §§ 1.803-1.809 would satisfy the requirements of 35 U.S.C. § 112, first paragraph, provided that Applicants submit an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that a deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. The Action further states that the instant specification must be amended to recite the date of the deposit and the complete name and address of the depository, and that the claims must be amended to recite the accession number.

Pursuant to the Examiner's request, Applicants' representative submits that Applicants deposited cDNA encoding human FGF-L polypeptide with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209. The deposit was accepted by the ATCC, an International Depository Authority, under the provisions of the Budapest Treaty, and the deposit was designated as PTA-1882. A copy of the ATCC receipt for this deposit, showing the patent deposit designation (Accession No. PTA-1882) and the date on which the deposit was received by the ATCC (May 17, 2000) is attached. Pursuant to 37 C.F.R. § 1.808(a)(2), the deposit was made under conditions that assure that all restrictions imposed by the depositors on the availability to the public of the deposited material would be irrevocably removed upon the granting of a patent relying on the deposited biological material. In making the deposit, Applicants acknowledged their responsibility, pursuant to 37 C.F.R. § 1.805, to provide a replacement or supplemental deposit if the depository possessing the deposit is unable to furnish samples thereof or is able to furnish samples thereof but the deposit has become contaminated or has lost its capability to function as described in the specification. With regard to the assertion that the date of the deposit and the complete name and address of the depository is not referred to in the body of the specification, Applicants respectfully direct the Examiner's attention to 77, lines 24-27 of the specification where Applicants disclose that a deposit of cDNA encoding human FGF-L polypeptide, subcloned into pGEM-T: JH3 (Promega; Madison, WI), and having Accession No. PTA-1882, was made with the American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209, on May 17, 2000. With regard to the assertion that the accession number of the deposit is not referred to in the claims, Applicants respectfully direct the Examiner's attention to claims 1(b) and 2(b)-2(d), as originally filed. Applicants contend that all the requirements of 37 C.F.R. §§ 1.801-1.809 have been met. *In re Lundak*, 225 U.S.P.Q. 90 (Fed. Cir. 1985). Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the claims do not place any limit on the number of nucleotide substitutions, deletions, insertions, or additions that may be made to the FGF-L molecules of the invention, the claimed genus of nucleic

acid molecules is highly variant. The Action also states that because one of ordinary skill in the art cannot envision the detailed structure of the genus of nucleic acid molecules encompassed by the claims, and the specification does not contain a sufficient recitation of distinguishing identifying characteristics of the genus, the specification does not meet the written description requirement for claiming such a genus.

Applicants have amended claim 1 to recite an isolated nucleic acid molecule comprising a nucleotide sequence as set forth in SEQ ID NO: 1; a nucleotide sequence comprising nucleotide residues 610 through 1242 of the nucleotide sequence set forth in SEQ ID NO: 1; a nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1882; a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of a nucleotide sequence comprising nucleotide residues 610 through 1242 of the nucleotide sequence set forth in SEQ ID NO: 1 or a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that the genus of molecules encompassed by amended claim 1 is not highly variant, as this claim does not encompass FGF-L molecules containing any number of nucleotide substitutions, and that one of ordinary skill in the art could readily determine the structure of the nucleic acid molecules falling within the scope of this claim. Applicants, therefore, submit that amended claim 1 satisfies the requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of this claim on § 112, first paragraph, grounds be withdrawn.

Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of SEQ ID NO: 1 or the DNA insert in ATCC Deposit No. PTA-1882 encoding a polypeptide fragment of SEQ ID NO: 2 of at least 50 amino acid residues; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of this nucleotide sequence; or a nucleotide sequence that is complementary to this nucleotide sequence. Applicants note that claim 2, as amended, no longer recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least 70 percent identical to the polypeptide of SEQ ID NO: 2; a nucleotide sequence encoding an allelic or splice variant of the nucleotide sequence of SEQ ID NO: 1, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1882, or of a nucleotide sequence recited in claim 2; or a region of the

nucleotide sequence of SEQ ID NO: 1, the DNA insert in ATCC Deposit No. PTA-1882, or a nucleotide sequence recited in claim 2 comprising a fragment of at least about 16 nucleotides. Applicants contend that the genus of molecules encompassed by amended claim 2 is not highly variant, as this claim does not encompass FGF-L molecules containing any number of nucleotide substitutions. Applicants also contend that because amended claim 2 recites only fragments of the disclosed human FGF-L nucleic acid molecule that encode an FGF-L polypeptide fragment of at least 50 amino acid residues, one of ordinary skill in the art could readily determine the structure of nucleic acid molecules falling within the scope of this claim. Applicants, therefore, submit that amended claim 2 satisfies the requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of this claim on § 112, first paragraph, grounds be withdrawn.

Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 85 percent identical to the polypeptide set forth in SEQ ID NO: 2; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 50 amino acid residues; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-terminal truncation, wherein the encoded polypeptide is at least 85 percent identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 50 amino acid residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants note that claim 3, as amended, no longer recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion; a fragment of a nucleotide sequence recited in claim 3 comprising at least 16 nucleotides; or a nucleotide sequence which hybridizes under at least moderately stringent conditions to the complement of a nucleotide sequence recited in claim 3. Applicants also note that the instant application teaches the nucleotide and amino acid sequences for human FGF-L polypeptide (Figures 1A-1B); that FGF-L shares a high degree of amino sequence identity with several other members of the FGF family of proteins (Figures 2-4 and page 74, lines 18-19); that regions in FGF-L polypeptide that are tolerable to conservative amino acid substitution can be

identified by performing sequence comparisons between FGF-L polypeptide and other related polypeptides (page 20, lines 5-9); and rubrics recognized in the art for making conservative amino acid substitutions (Table I; pages 19-20). Applicants contend, for example, that one of ordinary skill in the art could perform a sequence comparison of the human FGF-L polypeptide disclosed in the instant specification and the FGF-L ortholog disclosed by Koga *et al.* in order to determine the positions within the human FGF-L polypeptide sequence where substitutions, either conservative or nonconservative, would be tolerated, and that such a comparison would be well within the skill of one having ordinary skill in the art. In view of the teachings in the instant application and knowledge in the art at the time the instant application was filed, Applicants contend that one of ordinary skill in the art would understand the scope of species comprising the genus of FGF-L variants defined by claim 3, and that the inventors were in possession of the invention having said scope at the time the application was filed. Applicants, therefore, submit that amended claim 3 satisfies the requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of this claim on § 112, first paragraph, grounds be withdrawn.

The Office Action also asserts a rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that because the specification lacks sufficient guidance regarding the positions of FGF-L polypeptide that are essential for its biological activity, one of ordinary skill in the art would be left to extensive trial and error experimentation in order to identify polypeptides that retain FGF-L polypeptide function, and therefore, it would require undue experimentation to make and use nucleic acid molecules encoding such polypeptides.

As described above, Applicants have amended claims 1-3 so that they no longer recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least 70 percent identical to the polypeptide of SEQ ID NO: 2; a nucleotide sequence encoding an allelic or splice variant of the nucleotide sequence of SEQ ID NO: 1, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1882, or of a nucleotide sequence recited in claim 2; a region of the nucleotide sequence of SEQ ID NO: 1, the DNA insert in ATCC Deposit No. PTA-1882, a nucleotide sequence recited in claim 2 comprising a fragment of at least about 16 nucleotides; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino



acid insertion; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion; a fragment of a nucleotide sequence recited in claim 3 comprising at least 16 nucleotides; or a nucleotide sequence which hybridizes under at least moderately stringent conditions to the complement of a nucleotide sequence recited in claim 3. Applicants, therefore, contend that the claims, as amended, are not overly broad. Applicants also contend that, in view of the specification's teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to make and use the claimed invention, and therefore, Applicants respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

#### **4. Rejections of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 112, second paragraph**

The Office Action asserts a rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

The Action first asserts that claims 8 and 10 are indefinite for reciting the phrase “moderately or highly stringent conditions,” because the specification fails to precisely define “moderately or highly stringent conditions.” Applicants note that the specification defines the meaning of the terms “moderately stringent conditions” (page 16, lines 3-9) and “highly stringent conditions” (page 15, lines 1-8), and provides examples of each. However, in order to expedite prosecution of the pending claims to allowance, and in Applicants' view because it will have no substantive effect in the proper scope of the pending claims, Applicants have amended claims 1 and 2 to recite that the claimed nucleic acid molecules comprise a nucleotide sequence that “hybridizes under at least moderately stringent conditions,” and have amended claim 3 to delete the objected-to limitation. Applicants contend that claims 1-3, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 8 and 10 are indefinite for reciting the term “FGF-L polypeptide,” because the specification does not identify the material element or combination of elements that is definitive of an “FGF-L polypeptide,” and therefore, a skilled artisan would be

unable to determine what additional or material limitations are placed upon a claim by the presence of this element. Applicants note first that an explicit definition of “FGF-L polypeptide” is provided in the specification at page 9, lines 21-26, and contend that this definition controls the interpretation of the term “FGF-L polypeptide” as it is used in the claims of the instant application. Applicants contend, for example, that it would be apparent to one of ordinary skill in the art that a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 is a FGF-L polypeptide. Applicants further contend that it would be apparent to one of ordinary skill in the art that a polypeptide variant (*e.g.*, a polypeptide having at least one conservative amino acid substitution) of the amino acid sequence of SEQ ID NO: 2 is a FGF-L polypeptide, provided that the polypeptide variant has an activity of the polypeptide set forth in SEQ ID NO: 2. However, in order to expedite prosecution of the pending claims to allowance, and in Applicants’ view because it will have no substantive effect in the proper scope of the pending claims, Applicants have amended claim 8 to recite a process of producing a polypeptide encoded by the nucleic acid molecule of any of Claims 1, 2, or 3, and have amended claim 10 to recite that the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native FGF-L gene operatively linked to the nucleic acid molecule. Applicants note that an explicit definition of the term “FGF-L gene” is provided in the specification at page 7, lines 22-26. Applicants contend, therefore, that claims 8 and 10, as amended, are not indefinite, and respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 2-8, 10, 11, and 44 are indefinite for reciting the phrase “has an activity of the polypeptide set forth in . . . SEQ ID NO: 2,” because the specification does not identify the material element or combination of elements that is definitive of an “an activity of the polypeptide set forth in . . . SEQ ID NO: 2,” and therefore, a skilled artisan would be unable to determine what additional or material limitations are placed upon a claim by the presence of this element. While Applicants respectfully disagree with the assertion that this phrase is indefinite, in an effort to expedite the present application to allowance, Applicants have amended the pending claims to delete the objected-to phrase and instead affirmatively recite that FGF-L polypeptide variants or C- and/or N- terminally truncated FGF-L polypeptide variants must comprise at least 50 amino acid residues and that conservatively substituted FGF-L variants must be at least 85 percent identical to the polypeptide of SEQ ID NO: 2. Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 1-8, 10, 11, and 44 are indefinite for reciting the term “complementary to,” because it is unclear whether the claimed nucleic acid molecule is a full length complement of a recited nucleic acid molecule or complementary only to some portion of the recited nucleic acid molecule. Applicants respectfully disagree with the Action’s assertion that 1-3 are indefinite for reciting the term “complementary to.” Applicants contend that the nucleotide sequence complement of the nucleotide sequence 5’-A-G-C-T-A-G-C-T-3’, for example, is well understood in the art to be 5’-T-C-G-A-T-C-G-A-3’, rather than the nucleotide sequence 5’-T-C-G-A-T-C-G-3’ or some other portion of the nucleotide sequence 5’-T-C-G-A-T-C-G-A-3’. Applicants contend, therefore, that one of ordinary skill in the art would understand that a nucleotide sequence that is complementary to the nucleotide sequence of SEQ ID NO: 1 must be the same length as the nucleotide sequence of SEQ ID NO: 1 (*i.e.*, 1330 nucleotides). Moreover, Applicants contend that such a meaning is consistent with the meaning given to the term “complementary to” by Alberts *et al.*, *Molecular Biology of the Cell*, pp. 5-7 (Garland Publishing, Inc., 1994) (describing a complementary sequence as “a mold of the original,” such that the sequence of nucleotides in a nucleic acid molecule is *preserved* in its complementary strand). Applicants, therefore, respectfully contend that claims 1-3, as amended, fulfill the requirements of 35 U.S.C. § 112, first paragraph.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

#### **5. Rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 102**

The Office Action asserts a rejection of claims 3-6 and 8 under 35 U.S.C. § 102(a), as being anticipated by Koga *et al.*, 1999, *Biochem. Biophys. Res. Commun.* 261:756-65. The Action states that because the phrase “moderately or highly stringent conditions” is vague and indefinite, the nucleic acid molecule disclosed by Koga *et al.* would hybridize under moderately or highly stringent conditions to a nucleic acid molecule comprising a nucleotide sequence that is complementary to the nucleotide sequence of any of claims 3(a)-3(e). The Office Action also asserts a rejection of claims 1, 2, 4-6, 8, and 11 under 35 U.S.C. § 102(b), as being anticipated by Koga *et al.* The Action states that because the phrase “moderately or highly stringent conditions” is vague and indefinite, and Koga *et al.* disclose a nucleic acid molecule sharing a best local similarity of 74.2% with the nucleotide

sequence of SEQ ID NO: 1, the nucleic acid molecule disclosed by Koga *et al.* would hybridize under moderately or highly stringent conditions to a nucleic acid molecule comprising a nucleotide sequence that is complementary to the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1882. The Action also states that the nucleic acid molecule disclosed by Koga *et al.* comprises either a 16 nucleotide fragment of the nucleotide sequence of SEQ ID NO: 1 or a nucleotide sequence that is complementary to a 16 nucleotide fragment of the nucleotide sequence of SEQ ID NO: 1. The Action also states that the nucleic acid molecule disclosed by Koga *et al.* encodes a polypeptide that is at least 70% identical to the polypeptide as set forth in SEQ ID NO: 2 and comprises at least 25 amino acid residues. The Action further states that Koga *et al.* disclose a vector comprising the disclosed nucleic acid molecule, a eukaryotic host cell comprising the vector, and a process of producing the polypeptide encoded by the disclosed nucleic acid molecule comprising culturing the eukaryotic host cell.

As described in section 4 above, Applicants have amended claims 1 and 2 to recite that the claimed nucleic acid molecules comprise a nucleotide sequence that “hybridizes under at least moderately stringent conditions” to a recited nucleotide sequence. Applicants contend that claims 1 and 2, as amended, are not indefinite. In view of the specification’s teachings, Applicants contend that one of ordinary skill in the art would expect nucleic acid molecules that hybridize under moderately stringent conditions to differ in their nucleotide sequences by about 21% (page 16, lines 8-9). Applicants contend, therefore, that for a nucleic acid molecule to anticipate pending claims 1(e) or 2(b), it *must* comprise a nucleotide sequence that is about 79% identical to the nucleotide sequence comprising nucleotide residues 610 through 1242 of the nucleotide sequence set forth in SEQ ID NO: 1; a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2; or a nucleotide sequence of SEQ ID NO: 1 or the DNA insert in ATCC Deposit No. PTA-1882 encoding a polypeptide fragment of SEQ ID NO: 2 of at least 50 amino acid residues. As the Action suggests, even the most conserved *portion* of the nucleotide sequence disclosed by Koga *et al.* (*i.e.*, a region of 639 nucleotides) shares only 74.2% identity with the nucleotide sequence of SEQ ID NO: 1. Moreover, as shown in Exhibit F, the nucleotide sequence disclosed by Koga *et al.* shares an *overall* sequence identity of only 52.9% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit F was prepared using the application MacVector 7.1.1 at the default settings). Applicants contend that because the nucleic acid molecule disclosed by Koga *et al.* could not hybridize under at least

moderately stringent conditions to a nucleic acid molecule encompassed by the claims of the instant application, Koga *et al.* cannot anticipate claims directed to such FGF-L variants.

As described in section 3 above, Applicants have amended claims 2 and 3 so that they no longer recite an isolated nucleic acid molecule comprising either a region of the nucleotide sequence of SEQ ID NO: 1, the DNA insert in ATCC Deposit No. PTA-1882, or the nucleotide sequence of any of claims 2(a)-2(c) comprising a fragment of at least 16 nucleotides, or a nucleotide sequence of any of claims 3(a)-3(e) comprising a fragment of at least about 16 nucleotides. Applicants contend, therefore, that a 16 nucleotide fragment of the nucleotide sequence disclosed by Koga *et al.* or a nucleotide sequence that is complementary to such a fragment does not anticipate amended claims 2 and 3.

As also described in section 3 above, Applicants have amended claims 2 and 3 to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of SEQ ID NO: 1 or the DNA insert in ATCC Deposit No. PTA-1882 encoding a polypeptide fragment of SEQ ID NO: 2 of at least 50 amino acid residues; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 85 percent identical to the polypeptide of SEQ ID NO: 2; and a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 50 amino acid residues. Applicants contend that the nucleotide sequence disclosed by Koga *et al.* cannot anticipate claims directed to such FGF-L variants. For the Examiner's convenience, Applicants provide a sequence comparison of the FGF-L polypeptide disclosed by Koga *et al.* and the FGF-L polypeptide disclosed in the instant application (*see* Exhibit E).

Because Koga *et al.* does not disclose a nucleotide sequence that meets each and every limitation of the claimed invention, Koga *et al.* cannot anticipate claims 1-6, 8, or 11, as amended. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 1-8, 10, 11, and 44 under 35 U.S.C. § 102(e), as being anticipated by U.S. Patent Application Publication No. US 2002/0058036 A1 (the '036 publication), which published May 16, 2002 from U.S. Application No. 09/817,814, which was filed March 26, 2001 by Jeffers *et al.* The Action also asserts that the '036 publication is entitled to an effective filing date of July 27, 1999. The Action states that the '036 publication discloses a

nucleic acid molecule that shares 99.8% identity with the nucleotide sequence of SEQ ID NO: 1, and that this nucleic acid molecule encodes a polypeptide that shares 100% identity with the amino acid sequence of SEQ ID NO: 2. The Action also states that the '036 publication discloses a vector comprising the disclosed nucleic acid molecule, host cells transformed with this vector, polypeptides encoded by allelic variants, nucleic acid molecules containing single nucleotide polymorphisms and encoding polypeptides containing conservative amino acid substitutions, viral vectors, promoters, enhancers, and other expression control elements, and methods of producing the polypeptide encoded by the disclosed nucleic acid molecule using prokaryotic or eukaryotic host cells.

Applicants note that U.S. Application No. 09/817,814, which was filed on March 26, 2001, and upon which the '036 publication is based, is a continuation-in-part of U.S. Application No. 09/609,543, which was filed on July 3, 2000; that U.S. Application No. 09/609,543 is a continuation-in-part of U.S. Application No. 09/494,585, which was filed on January 31, 2000; and that U.S. Application No. 09/494,585 claims the benefit of U.S. Provisional Application No. 60/145,899, which was filed on July 27, 1999. Applicants also note that while the Examiner provided a copy of the '036 publication with the instant Action, Applicants have not had access to U.S. Application Nos. 09/609,543 and 09/494,585; or U.S. Provisional Application No. 60/145,899, from which U.S. Application No. 09/817,814 claims the benefit of priority, and upon which instant rejection depends.

Applicants contend that as between the U.S. Patent Office and Applicants, the U.S. Patent Office is in the best position to demonstrate that the subject matter which forms the basis of the instant rejection (*i.e.*, the full-length nucleotide sequence of FGF-L polypeptide), and which is disclosed in U.S. Application No. 09/817,814, is (if it is) also disclosed in U.S. Application Nos. 09/609,543 and 09/494,585; and U.S. Provisional Application No. 60/145,899. Pursuant to 37 C.F.R. § 104(d)(2), Applicants request that the Examiner make a determination as to whether the full-length nucleotide sequence of FGF-L polypeptide is disclosed in U.S. Application Nos. 09/609,543 and 09/494,585; and U.S. Provisional Application No. 60/145,899. Applicants contend that in absence of such a determination, the '036 publication is only entitled to the filing date of U.S. Application No. 09/817,814 (*i.e.*, March 26, 2001), and, therefore, that this reference is not in the prior art to the instant application under 35 U.S.C. § 102. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 1-5 and 7 under 35 U.S.C. § 102(b), as

being anticipated by Hillier *et al.* (GenBank Accession No. AA232729). The Action states that Hillier *et al.* disclose a nucleic acid molecule that is encompassed by claims 1(d), 1(e), 2(c)-2(f), and 3(e)-3(h). The Action also states that Hillier *et al.* disclose a vector comprising the disclosed nucleic acid molecule and a prokaryotic host cell comprising the vector. The Action also states that since claim 2(c) does not specify any particular 25 amino acids and any 25 amino acid polypeptide would be antigenic, Hillier *et al.* disclose a nucleic acid molecule encoding a polypeptide fragment of at least 25 amino acid residues, wherein the polypeptide fragment is antigenic. The Action further states that claim 3(e) encompasses essentially any and all polypeptides.

As described in section 3 above, Applicants have amended claim 1 to recite an isolated nucleic acid molecule comprising a nucleotide sequence as set forth in SEQ ID NO: 1; a nucleotide sequence comprising nucleotide residues 610 through 1242 of the nucleotide sequence set forth in SEQ ID NO: 1; a nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1882; a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of a nucleotide sequence comprising nucleotide residues 610 through 1242 of the nucleotide sequence set forth in SEQ ID NO: 1 or a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2; or a nucleotide sequence that is complementary to any of these nucleotide sequences. As shown in Exhibit G, while the nucleotide sequence disclosed by Hillier *et al.* comprises nucleotide residues 1 through 496 of the nucleotide sequence set forth in SEQ ID NO: 1, the FGF-L open reading frame comprises nucleotide residues 610 through 1242. Applicants contend that because the nucleotide sequence disclosed by Hillier *et al.* lacks any portion of the FGF-L open reading frame, Hillier *et al.* cannot anticipate claim 1.

As described in section 3 above, Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of SEQ ID NO: 1 or the DNA insert in ATCC Deposit No. PTA-1882 encoding a polypeptide fragment of SEQ ID NO: 2 of at least 50 amino acid residues; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of this nucleotide sequence; or a nucleotide sequence that is complementary to this nucleotide sequence. Applicants contend that because amended claim 2 is directed to an isolated nucleic acid that encodes at least a portion of the FGF-L polypeptide, and the nucleotide sequence disclosed by Hillier *et al.* lacks any portion of the FGF-L open reading frame,

Hillier *et al.* cannot anticipate claim 2.

As described in section 3 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 85 percent identical to the polypeptide set forth in SEQ ID NO: 2; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 50 amino acid residues; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-terminal truncation, wherein the encoded polypeptide is at least 85 percent identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 50 amino acid residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that claim 3, as amended, does not encompass essentially any and all polypeptides. Applicants also contend that because amended claim 3 is directed to an isolated nucleic acid that encodes at least a portion of the FGF-L polypeptide, and the nucleotide sequence disclosed by Hillier *et al.* lacks any portion of the FGF-L open reading frame, Hillier *et al.* cannot anticipate claim 2.

Because Hillier *et al.* does not disclose a nucleotide sequence that meets each and every limitation of the claimed invention, Hillier *et al.* cannot anticipate claims 1-5 and 7, as amended. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 3-8, 10 and 44 under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent No. 5,693,775 (the '775 Patent), which issued to Nathans *et al.* on December 2, 1997. The Action states that because claim 3(e) encompasses essentially any and all polypeptides, the '775 Patent discloses a nucleic acid molecule that is encompassed by claim 3(e). The Action also states that the '775 Patent discloses a vector comprising the disclosed nucleic acid molecule, eukaryotic and prokaryotic host cells comprising the vector, and methods of making the polypeptide encoded by the disclosed nucleic acid molecule.

As described above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 85 percent identical to the polypeptide set forth in SEQ ID NO: 2; a nucleotide sequence encoding a



polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 50 amino acid residues; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-terminal truncation, wherein the encoded polypeptide is at least 85 percent identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 50 amino acid residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because claim 3, as amended, does not encompass essentially any and all polypeptides, the nucleotide sequence disclosed by Nathans *et al.* cannot anticipate claims 3-8, 10 and 44. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

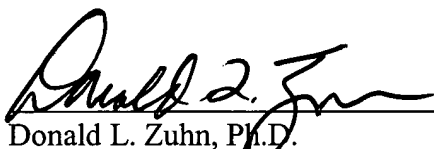
### **CONCLUSIONS**

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Romeo believes it to be helpful, he is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,  
**McDonnell Boehnen Hulbert & Berghoff**

Dated: July 14, 2003

By:   
Donald L. Zuhn, Ph.D.  
Reg. No. 48,710

**ATCC**

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-365-2745

**BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF  
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE****INTERNATIONAL FORM****RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3  
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2****To: (Name and Address of Depositor or Attorney)**

Amgen, Inc.  
Attn: Dawn Pohl  
One Amgen Center Drive, M/S 9-1-C  
Thousand Oaks, CA 91320-1799

**Deposited on Behalf of: Amgen, Inc.****Identification Reference by Depositor:**

Zhvt-003594, the cDNA of a human FGF-9 related molecule  
cloned into plasmid vector pGEM-T: JH3

**Patent Deposit Designation**

PTA-1882

The deposit was accompanied by:     a scientific description     a proposed taxonomic description indicated above.

The deposit was received May 17, 2000 by this International Depository Authority and has been accepted.

**AT YOUR REQUEST:**   X   We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested May 25, 2000. On that date, the culture was viable.

**International Depository Authority:** American Type Culture Collection, Manassas, VA 20110-2209 USA.

**Signature of person having authority to represent ATCC:**

  
Barbara E. Coupé, Administrator, Patent Depository

**Date:** May 30, 2000**cc: Richard J. Mazza (Ref: Docket or Case No.: A-668-P)**

## EXHIBIT A

	10	20	30	40	50
SEQ 1	TACACGGCCGCGAGCTGAACAGCATCACCGCTGTCCCAAGGACAACCCCAA				
	ATGTGCCGGCGTCGACTTGTCTAGTGGCGACAGGGTTCCTGTTGGGGTT				
	60	70	80	90	100
SEQ 1	AGAGGGGCCTCGACTGCACCTCCTCGAAGTTGCTGGCTGGCTTTGGCAAG				
	TCTCCCCGAGCTGACGTGGAGGAGCTTCAACGACCGACCGAAACCGTTC				
	110	120	130	140	150
SEQ 1	TGCAGGAATGGTGTGTTTTGTGAGGGCATGGATGGAGAAGTGCCAAGGGCCC				
	ACGTCCTTACCACAAAACTCCCGTACCTACCTCTTCACGGTTCCCGGG				
	160	170	180	190	200
SEQ 1	CTGTTTGGTCACTTCCGAAGAGCAAAAACGTGTTGAGAGGAGACCGGTTT				
	GACAAACCAGTGAAGGCTTCTCGTTTTTGCACAACCTCTCCTCTGGCCAAA				
	210	220	230	240	250
SEQ 1	AAGATTTCAAACAGAACCTCCCCAGCGCGCATGAAAGGACTTGATTAGCA				
	TTCTAAAGTTTGTCTTGGAGGGGTCGCGCGTACTTTCCTGAACTAATCGT				
	260	270	280	290	300
SEQ 1	TATGTCAAGAGGACCCGCTTATATACTCGGTGTGTATGTACACAGGACTC				
	ATACAGTTCTCCTGGGCGAATATATGAGCCACACATACATGTGTCTGAG				
	310	320	330	340	350
SEQ 1	TGATCTGATCAGTTTGCGGAATTGGAGCCCCAGCCAACAGCCCTAGTCCT				
	ACTAGACTAGTCAAACGCCTTAACCTCGGGGTCGGTTGTCGGGATCAGGA				
	360	370	380	390	400
SEQ 1	AGTATTGGCAGCGGCAGCTATAGATATTTCTGCAGAGCCAGCAGCCGGCT				
	TCATAACCGTCGCCGTCGATATCTATAAAGACGTCTCGGTCTGTCGGCCGA				
	410	420	430	440	450
SEQ 1	CCCACCTACCCAAGGAGAGAAGATCGCTCCAAGACAGTGAGAGCTTCCCT				
	GGGTGGATGGGTTCCCTCTCTTCTAGCGAGGTTCTGTCACTCTCGAAGGGA				
	460	470	480	490	500
SEQ 1	GCCATTTCAGTGCAAAGTCCCTCCGGAGCGACCTCAGAGGAGTAACCGGG				
	CGGTAAAGTCACGTTTCAGGGAGGCCTCGCTGGAGTCTCCTCATTGGCCC				
	510	520	530	540	550
SEQ 1	CCTTAACTTTTTGCGCTCGTTTTGCTATAATTTTTCTCTATCCACCTCCA				
	GGAATTGAAAAACGCGAGCAAAACGATATTAAAAAGAGATAGGTGGAGGT				

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          560      570      580      590      600
SEQ 1      TCCCCACCCCACTCTTTACTGGGGGGTCTTTTGTGTTCCGGATC
            AGGGTGGGGGTGTTGTGAGAAATGACCCCCCAGAAAACACAAGGCCTAG

          610      620      630      640      650
SEQ 1      TCCCCCTCCATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT
            AGGGGGAGGTACCGAGGGAATCGGCTTCAGCCCCGAAAGACCCGCCGGA

1. FIG. 1
[ 2532 ]
          10      20      30      40
            ATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT>
            |||||
SEQ 1      ATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT

          660      670      680      690      700
SEQ 1      GGAGGGCTTGGGCCAGCAGGTGGGTTTCGCATTTCTGTTGCCTCCTGCCG
            CCTCCGAACCCGGTCGTCCACCCAAGCGTAAAGGACAACGGAGGACGGC

1. FIG. 1
[ 2532 ]
          50      60      70      80      90
            GGAGGGCTTGGGCCAGCAGGTGGGTTTCGCATTTCTGTTGCCTCCTGCCG>
            |||||
SEQ 1      GGAGGGCTTGGGCCAGCAGGTGGGTTTCGCATTTCTGTTGCCTCCTGCCG

          710      720      730      740      750
SEQ 1      GGGAGCGGCCGCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC
            CCTCGCCGGCGGCGACGACCCGCTCGCGTCCTCGCGCCGCTCGCCTCG

1. FIG. 1
[ 2532 ]
          100     110     120     130     140
            GGGAGCGGCCGCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC>
            |||||
SEQ 1      GGGAGCGGCCGCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC

          760      770      780      790      800
SEQ 1      GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT
            CGGGCGCCGCCGCGCCCCGACGCGTCGACCGGTGGACGTGCCGTAGGA

1. FIG. 1
[ 2532 ]
          150     160     170     180     190
            GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT>
            |||||
SEQ 1      GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT

          810      820      830      840      850
SEQ 1      GCGCCGCCGGCAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC
            CGCGGCGGCCGTCGAGATAACGGCGTGGCCGAAGGTGGACGTCTAGGACG

1. FIG. 1
[ 2532 ]
          200     210     220     230     240
            GCGCCGCCGGCAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC>
            |||||
SEQ 1      GCGCCGCCGGCAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC

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      860      870      880      890      900
SEQ 1  CCGACGGCAGCGTGCAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC
      GGCTGCCGTCGCACGTCCCGTGGGCCGTCCTGGTGTCTGGAGAAGCCATAG

1. FIG. 1      250      260      270      280      290
[ 2532 ]  CCGACGGCAGCGTGCAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC>
      |||
SEQ 1  CCGACGGCAGCGTGCAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC

      910      920      930      940      950
SEQ 1  TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA
      AACCTTAAGTAGTCACACCGTCACCCTGACCAGTCATAATCTCCACACCT

1. FIG. 1      300      310      320      330      340
[ 2532 ]  TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA>
      |||
SEQ 1  TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA

      960      970      980      990      1000
SEQ 1  CAGTGGTCTCTATCTTTGGAATGAATGACAAAGGAGAACTCTATGGATCAG
      GTCACCAGAGATAGAACCTTACTTACTGTTTCTCTTGAGATACCTAGTC

1. FIG. 1      350      360      370      380      390
[ 2532 ]  CAGTGGTCTCTATCTTTGGAATGAATGACAAAGGAGAACTCTATGGATCAG>
      |||
SEQ 1  CAGTGGTCTCTATCTTTGGAATGAATGACAAAGGAGAACTCTATGGATCAG

      1010      1020      1030      1040      1050
SEQ 1  AGAAACTTACTTCCGAATGCATCTTTAGGGAGCAGTTTGAAGAGAACTGG
      TCTTTGAATGAAGGCTTACGTAGAAATCCCTCGTCAAACCTTCTCTTGACC

1. FIG. 1      400      410      420      430      440
[ 2532 ]  AGAAACTTACTTCCGAATGCATCTTTAGGGAGCAGTTTGAAGAGAACTGG>
      |||
SEQ 1  AGAAACTTACTTCCGAATGCATCTTTAGGGAGCAGTTTGAAGAGAACTGG

      1060      1070      1080      1090      1100
SEQ 1  TATAACACCTATTCATCTAACATATATAAACATGGAGACACTGGCCGCAG
      ATATTGTGGATAAGTAGATTGTATATATTTGTACCTCTGTGACCGGCGTC

1. FIG. 1      450      460      470      480      490
[ 2532 ]  TATAACACCTATTCATCTAACATATATAAACATGGAGACACTGGCCGCAG>
      |||
SEQ 1  TATAACACCTATTCATCTAACATATATAAACATGGAGACACTGGCCGCAG

      1110      1120      1130      1140      1150
SEQ 1  GTATTTTGTGGCACTTAACAAAGACGGAACCTCAAGAGATGGCGCCAGGT
      CATAAAACACCGTGAATTGTTTCTGCCTTGAGGTTCTCTACCGCGGTCCA

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1. FIG. 1          500      510      520      530      540
[ 2532 ]          GTATTTTGTGGCACTTAACAAAGACGGAACCTCCAAGAGATGGCGCCAGGT>
                  |||
SEQ 1             GTATTTTGTGGCACTTAACAAAGACGGAACCTCCAAGAGATGGCGCCAGGT

                  1160      1170      1180      1190      1200
SEQ 1             CCAAGAGGCATCAGAAATTTACACATTTCTTACCTAGACCAGTGGATCCA
                  GGTTCCTCCGTAGTCTTTAAATGTGTAAAGAATGGATCTGGTCACCTAGGT

1. FIG. 1          550      560      570      580      590
[ 2532 ]          CCAAGAGGCATCAGAAATTTACACATTTCTTACCTAGACCAGTGGATCCA>
                  |||
SEQ 1             CCAAGAGGCATCAGAAATTTACACATTTCTTACCTAGACCAGTGGATCCA

                  1210      1220      1230      1240      1250
SEQ 1             GAAAGAGTTCCAGAATTGTACAAGGACCTACTGATGTACACTTGAAGTGC
                  CTTTCTCAAGGTCTTAACATGTTCTGATGACTACATGTGAACTTCACG

1. FIG. 1          600      610      620      630
[ 2532 ]          GAAAGAGTTCCAGAATTGTACAAGGACCTACTGATGTACACT>
                  |||
SEQ 1             GAAAGAGTTCCAGAATTGTACAAGGACCTACTGATGTACACT

                  1260      1270      1280      1290      1300
SEQ 1             GATAGTGACATTATGGAAGAGTCAAACCACAACCATTCTTTCTTGTCATA
                  CTATCACTGTAATACCTTCTCAGTTTGGTGTGGTAAGAAAGAACAGTAT

                  1310      1320      1330
SEQ 1             GTTCCCATCATAAAAATAATGACCCAAGCAG
                  CAAGGGTAGTATTTTATTACTGGGTTTCGTC

```

## EXHIBIT B

Aligned Length = 212    Gaps = 2  
Identities = 144 (68%)    Similarities = 26 (12%)

```
huFGF-L   1 MAPLAEVGGFLGGLEGLGQQVGSFLLPPAGERPPLLGERSSAAER-SAR  49
FGF-9     1 MAPLGEVGNVFGVQDAVPFGNVPVLP---VDSPVLLSDHLGQSEAGGLP  46
          *****
          *   *   *   *   *   *   *   *   *   *   *   *   *   *   *   *

huFGF-L   50 GGPAAQLAHLHGILRRRQLYCRTGFHLQILPDGSVQGTRQDHSFLFGILE  99
FGF-9     47 RGPVATDLHLKGILRRRQLYCRTGFHLEIFPNGTIQGTRKDHSRFGILE  96
          **   *   *   *   *   *   *   *   *   *   *   *   *   *   *   *

huFGF-L   100 FISVAVGLVSIRGVDSGLYLGMDKGEYSEKLTSECIFREQFEENWYN  149
FGF-9     97 FISIAVGLVSIRGVDSGLYLGMDKGEYSEKLTQECVFREQFEENWYN  146
          ***   *   *   *   *   *   *   *   *   *   *   *   *   *   *   *

huFGF-L   150 TYSSNIYKHGDTGRRYFVALNKDGTGPRDGARSKRHQKFTHFLPRPVDPER  199
FGF-9     147 TYSSNLYKHVDTGRRYYVALNKDGTGPRGTRTKRHQKFTHFLPRPVDPK  196
          *****   *   *   *   *   *   *   *   *   *   *   *   *   *

huFGF-L   200 VPELYKDILMYT 211
FGF-9     197 VPELYKDILSQS 208
          *****   *   *
```

Aligned Length = 211    Gaps = 1  
Identities = 131 (62%)    Similarities = 30 (14%)

```
huFGF-L   1 MAPLAEVGGFLGGLEGLGQQVGSFLLPPAGERPPLLGERSSAAERSARG  50
FGF-16     1 MAEVGGVFASLDWDLHGFSSSLGNVPLADSPGFLNERLGQIEGKLQR  47
          *****   *   *   *   *   *   *   *   *   *   *   *   *

huFGF-L   51 GPGAAQLAHLHGILRRRQLYCRTGFHLQILPDGSVQGTRQDHSFLFGILEF  100
FGF-16     48 G-SPTDFAHLKGILRRRQLYCRTGFHLEIFPNGTVHGTRHDHSRFGILEF  96
          *   *   *   *   *   *   *   *   *   *   *   *   *   *   *

huFGF-L   101 ISVAVGLVSIRGVDSGLYLGMDKGEYSEKLTSECIFREQFEENWYNT  150
FGF-16     97 ISLAVGLISIRGVDSGLYLGMDKGEYSEKLTRECVFREQFEENWYNT  146
          **   *   *   *   *   *   *   *   *   *   *   *   *   *   *

huFGF-L   151 YSSNIYKHGDTGRRYFVALNKDGTGPRDGARSKRHQKFTHFLPRPVDPERV  200
FGF-16     147 YASTLYKHSDSERQYYVALNKDGSPREGYRTKRHQKFTHFLPRPVDPSKL  196
          *   *   *   *   *   *   *   *   *   *   *   *   *   *   *

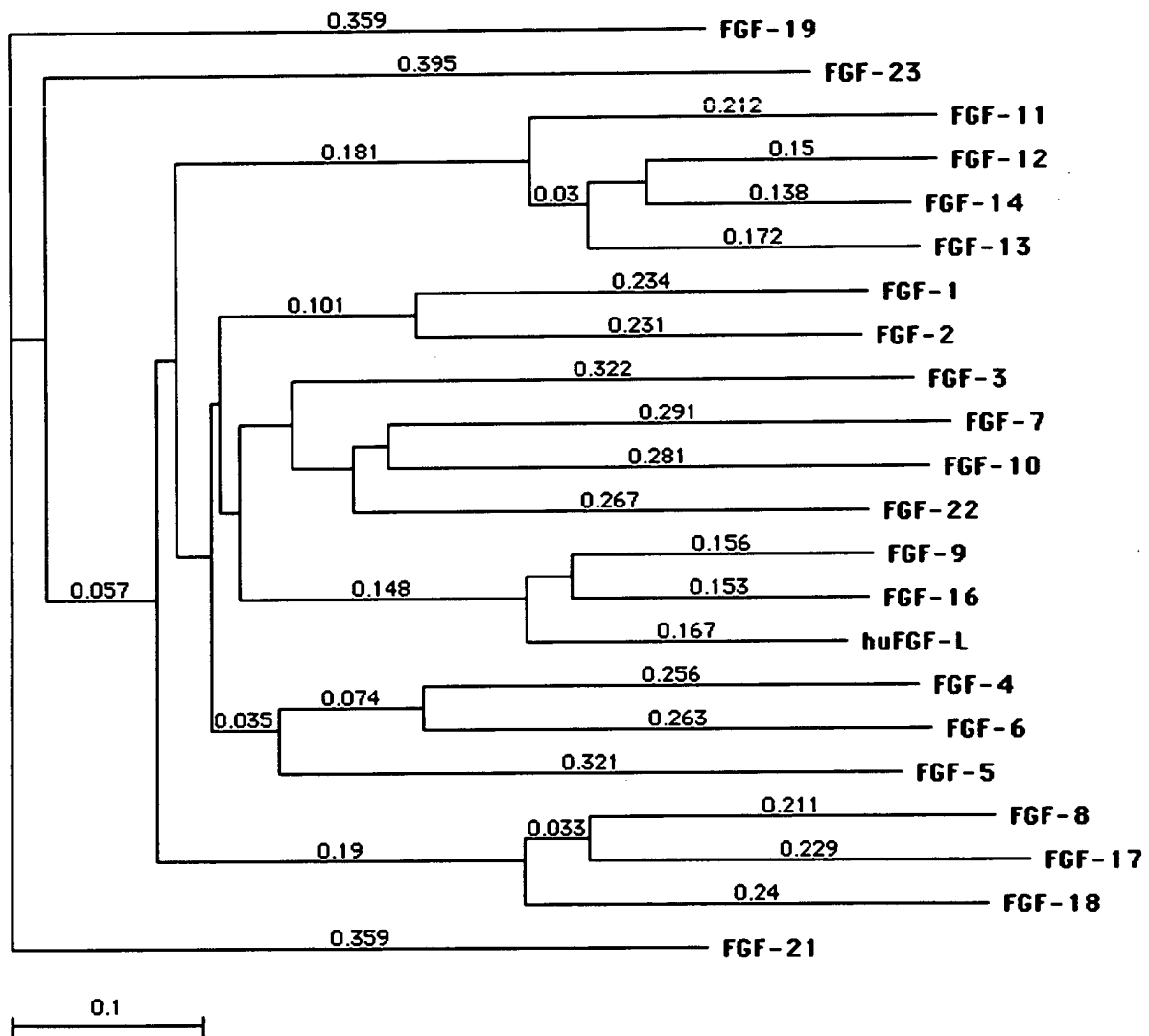
huFGF-L   201 PELYKDILMYT 211
FGF-16     197 PSMSRDLFHYR 207
          *   *   *   *
```

### Exhibit C

ClustalW (v1.4) Multiple Alignment Parameters:

Open Gap Penalty = 10.0; Extend Gap Penalty = 0.0; Delay Divergent = 40%

Gap Distance = 8; Similarity Matrix = blosum





## EXHIBIT D

Sequences producing significant alignments:					Score (bits)	E Value
gi	9789947	ref NP_062825.1	fibroblast growth factor 20 [Ho...		345	2e-94
gi	26342460	dbj BAC34892.1	unnamed protein product [Mus mu...		341	4e-93
gi	13027408	ref NP_076451.1	fibroblast growth factor 20 [R...		337	8e-92
gi	13447396	ref NP_085113.1	fibroblast growth factor 20 [M...		337	1e-91
gi	7512161	pir JC7082	fibroblast somatotropin-20 - African...		304	5e-82
gi	2494456	sp Q91875 FGF9_XENLA	GLIA-ACTIVATING FACTOR PREC...		283	9e-76
gi	30038758	dbj BAC75716.1	fibroblast groth factor 9 [Gall...		281	4e-75
gi	4503707	ref NP_002001.1	fibroblast growth factor 9 prec...		279	2e-74
gi	7305057	ref NP_038546.1	fibroblast growth factor 9; gli...		279	2e-74
gi	13399478	pdb 1G82 A	Chain A, Structure Of Fibroblast Gro...		279	3e-74
gi	25742766	ref NP_037084.1	fibroblast growth factor 9 [Ra...		279	3e-74
gi	15487681	gb AAK61609.2	fibroblast growth factor 9 [Sus ...		278	4e-74
gi	14278240	pdb 1IHK A	Chain A, Crystal Structure Of Fibrob...		277	7e-74
gi	11093923	gb AAG29501.1	FGF-16 protein [Mus musculus]		254	8e-67
gi	4503691	ref NP_003859.1	fibroblast growth factor 16 [Ho...		253	1e-66
gi	11177916	ref NP_068639.1	fibroblast growth factor 16 [R...		253	1e-66
gi	13449275	ref NP_085117.1	fibroblast growth factor 16 [M...		251	6e-66
gi	19912822	dbj BAB88673.1	fibroblast growth factor 9/16/2...		140	1e-32
gi	24137641	dbj BAC22069.1	fibroblast growth factor 9/16/2...		137	9e-32
gi	19031193	gb AAK59700.1	fibroblast growth factor 10 [Amb...		129	3e-29
gi	6911123	gb AAF31393.1 AF199606_1	fibroblast growth facto...		126	2e-28
gi	1345995	sp P48801 FGF3_CHICK	Fibroblast growth factor-3 ...		126	3e-28
gi	28872756	ref NP_787125.1	fibroblast growth factor 14 is...		125	6e-28
gi	2911146	dbj BAA24945.1	fibroblast growth factor 10 [Gal...		124	7e-28
gi	3299784	dbj BAA31543.1	FHF-4b [Mus musculus] >gi 329978...		124	7e-28
gi	19070525	gb AAL83904.1 AF348523_1	fibroblast growth fact...		124	8e-28
gi	4758368	ref NP_004106.1	fibroblast growth factor 14 iso...		124	9e-28
gi	19224657	ref NP_071559.2	fibroblast growth factor 14; F...		124	9e-28
gi	6911121	gb AAF31392.1 AF199605_1	fibroblast growth facto...		124	1e-27
gi	4758360	ref NP_004456.1	fibroblast growth factor 10 pre...		124	1e-27
gi	6978837	ref NP_037083.1	fibroblast growth factor 10 [Ra...		124	1e-27
gi	14388499	dbj BAB60779.1	hypothetical protein [Macaca fa...		124	1e-27
gi	6753848	ref NP_034331.1	fibroblast growth factor 14 [Mu...		124	1e-27
gi	21314400	gb AAM46926.1 AF508782_1	fibroblast growth fact...		123	2e-27
gi	28949024	pdb 1NUN A	Chain A, Crystal Structure Analysis ...		122	3e-27
gi	544288	sp P36386 FGF3_XENLA	FIBROBLAST GROWTH FACTOR-3 P...		122	4e-27
gi	7106313	ref NP_032028.1	fibroblast growth factor 10 [Mu...		122	5e-27
gi	18543363	ref NP_570107.1	fibroblast growth factor 22 [R...		121	7e-27
gi	69035	pir TVHUF5	fibroblast growth factor 5 - human >gi...		121	7e-27
gi	11559990	ref NP_071547.1	fibroblast growth factor FGF-5...		121	7e-27
gi	4758370	ref NP_004455.1	fibroblast growth factor 5 isof...		121	8e-27
gi	22655537	gb AAN04097.1	fibroblast growth factor-5 [Homo...		121	8e-27
gi	6753854	ref NP_034333.1	fibroblast growth factor 5 [Mus...		121	9e-27
gi	6708457	gb AAF25944.1 AF213396_1	fibroblast growth facto...		121	9e-27
gi	13637763	sp P12034 FGF5_HUMAN	Fibroblast growth factor-5...		121	9e-27
gi	4512022	gb AAD21576.1	fibroblast growth factor 13 isofo...		120	1e-26
gi	15705915	gb AAL05875.1 AF411527_1	keratinocyte growth fa...		120	2e-26
gi	13626683	sp P79150 FGF7_CANFA	Keratinocyte growth factor...		120	2e-26
gi	31542809	ref NP_034330.2	fibroblast growth factor 13 [M...		119	3e-26
gi	2494462	sp P70377 FGFD_MOUSE	FIBROBLAST GROWTH FACTOR-13...		119	3e-26
gi	4758366	ref NP_004105.1	fibroblast growth factor 13 iso...		119	3e-26

gi	4503705	ref	NP_002000.1	fibroblast growth factor 7 prec...	119	3e-26
gi	430968	gb	AAA67335.1	human keratinocyte growth factor	119	3e-26
gi	2444477	gb	AAB71606.1	fibroblast growth factor-related ...	119	3e-26
gi	6911131	gb	AAF31397.1	AF199610_1 fibroblast growth facto...	119	4e-26
gi	1346000	sp	P48808	FGF7_SHEEP KERATINOCYTE GROWTH FACTOR ...	119	4e-26
gi	12963627	ref	NP_075793.1	fibroblast growth factor 22 [M...	118	6e-26
gi	28191242	gb	AAO33291.1	fibroblast growth factor-like pr...	118	6e-26
gi	16758168	ref	NP_445880.1	fibroblast growth factor 13 [R...	117	1e-25
gi	18677745	ref	NP_570830.1	fibroblast growth factor 3 [Ra...	117	2e-25
gi	16306543	ref	NP_378668.1	fibroblast growth factor 13 is...	117	2e-25
gi	6679783	ref	NP_032033.1	fibroblast growth factor 3 [Mus...	116	3e-25
gi	18490696	gb	AAH22524.1	Unknown (protein for MGC:26659) ...	115	4e-25
gi	21614511	ref	NP_004104.3	fibroblast growth factor 12 is...	115	5e-25
gi	4885233	ref	NP_005238.1	fibroblast growth factor 3 prec...	115	5e-25
gi	13626616	sp	Q9N198	FGF7_PIG Keratinocyte growth factor p...	115	7e-25
gi	11136630	ref	NP_066360.1	fibroblast growth factor 12 is...	115	7e-25
gi	6911116	gb	AAF31390.1	AF199602_1 fibroblast growth facto...	114	7e-25
gi	18677741	ref	NP_570827.1	fibroblast growth factor 12; f...	114	7e-25
gi	2444479	gb	AAB71607.1	fibroblast growth factor-related ...	114	8e-25
gi	4512020	gb	AAD21575.1	fibroblast growth factor 12 isofo...	114	1e-24
gi	7438523	pir	JG0184	fibroblast growth factor - human	114	1e-24
gi	5442453	gb	AAB18786.3	fibroblast growth factor [Homo sa...	112	4e-24
gi	16305071	gb	AAL16959.1	AF360986_1 fibroblast growth fact...	112	4e-24
gi	6980587	pdb	1QQI	A Chain A, The Crystal Structure Of Fib...	112	5e-24
gi	1749791	emb	CAA94240.1	fibroblast growth factor 12 [Hom...	112	5e-24
gi	18858671	ref	NP_571366.1	fibroblast growth factor 3 [Da...	110	1e-23
gi	16226033	gb	AAL16059.1	keratinocyte growth factor FGF-7...	110	1e-23
gi	7438522	pir	S26049	fibroblast growth factor 7 precursor...	108	7e-23
gi	27464175	gb	AAO15997.1	fibroblast growth factor 6 [Dani...	108	8e-23
gi	25396669	pir	H88481	protein let-756 [imported] - Caenor...	107	1e-22
gi	3980190	emb	CAA76422.1	fibroblast growth factor 6-relat...	107	2e-22
gi	1346001	sp	P48805	FGFA_XENLA Fibroblast growth factor-4-...	107	2e-22
gi	1749789	emb	CAA94239.1	fibroblast growth factor 11 [Hom...	107	2e-22
gi	11559943	ref	NP_071518.1	fibroblast growth factor 7 [Ra...	107	2e-22
gi	6679785	ref	NP_032034.1	fibroblast growth factor 7; Ker...	106	2e-22
gi	6980585	pdb	1QQK	A Chain A, The Crystal Structure Of Fib...	106	2e-22
gi	16305079	gb	AAL16963.1	AF360990_1 fibroblast growth fact...	106	3e-22
gi	6714538	dbj	BAA89483.1	FGF-14C (FHF-4C) [Mus musculus]	105	4e-22
gi	4758362	ref	NP_004103.1	fibroblast growth factor 11; fi...	105	4e-22
gi	15147343	ref	NP_066276.2	fibroblast growth factor 6 pre...	105	5e-22
gi	32491	emb	CAA45054.1	hst-2 (FGF-6) [Homo sapiens]	105	7e-22
gi	18677743	ref	NP_570829.1	fibroblast growth factor 11 [R...	104	1e-21
gi	6753844	ref	NP_034328.1	fibroblast growth factor 11 [Mu...	104	1e-21
gi	18858673	ref	NP_571710.1	fibroblast growth factor 4 [Da...	104	1e-21
gi	24137647	dbj	BAC22072.1	fibroblast growth factor 11/12/...	103	1e-21
gi	24571204	gb	AAN62915.1	fibroblast growth factor 10 [Dan...	103	2e-21
gi	18777759	ref	NP_571983.1	fibroblast growth factor 6 [Ra...	103	2e-21
gi	1346002	sp	P48806	FGFB_XENLA Fibroblast growth factor-4-...	103	2e-21
gi	17554196	ref	NP_498403.1	Lethal-756, essential fibrobla...	102	3e-21

## EXHIBIT E

Aligned Length = 211 Gaps = 2

Identities = 170 (80%) Similarities = 21 (9%)

```
huFGF-L AA      1 MAPLAEVGGFLGGLEGLGQQVGSFLLPPAGERPPLLGERRSAAERSARG 50
AB01265_AA      1 MAPLADVGTFLGGYDALG-QVGSFLLPPAKDSPLLFNDPLAQSERLSRS 49
                *****
                . ** ***** . * * .. . ** . *

huFGF-L AA      51 GPGAAQLAHLHGILRRRQLYCRTGFHLQILPDGSVQGTRQDHSFLFGILEF 100
AB01265_AA      50 AP--SDLSHLQGILRRRQLYCRTGFHLQILPDGNVQGTRQDHSRFGILEF 97
                * . *. ***** *****

huFGF-L AA      101 ISVAVGLVSIRGVDSGLYLGMNDKGELYGSEKLTSECIFREQFEENWYNT 150
AB01265_AA      98 ISVAIGLVSIRGVDTGLYLGMNDKGELFGSEKLTSECIFREQFEENWYNT 147
                ****.*****.*****.*****.*****

huFGF-L AA      151 YSSNIYKHGDTGRRYFVALNKDGTPRDGARSKRHQKFTHFLRPVDPERV 200
AB01265_AA      148 YSSNLYKHGDSGRRYFVALNKDGTPRDGTRAKRHQKFTHFLRPVDPEKV 197
                ****.*****.*****.*****.*****.

huFGF-L AA      201 PELYKDLLMYT 211
AB01265_AA      198 PELYKDLMGYS 208
                ***** . *
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# EXHIBIT F

	10	20	30	40	50
huFGF-L	TACACGGCCGCGAGCTGAACAGCATCACCGCTGTCCCAAGGACAACCCCAA				
	ATGTGCCGGCGTCGACTTGTTCGTAGTGGCGACAGGGTTCCTGTTGGGGTT				

	60	70	80	90	100
huFGF-L	AGAGGGGCCTCGACTGCACCTCCTCGAAGTTGCTGGCTGGCTTTGGCAAG				
	TCTCCCCGGAGCTGACGTGGAGGAGCTTCAACGACCGACCGAAACCGTTC				

1. AB01265					
[ 1790 ]					GAAT>
huFGF-L					CAAG

	110	120	130	140	150
huFGF-L	TGCAGGAATGGTGTGTTTTGTGAGGGCATGGATGGAGAAGTGCCAAGGGCCC				
	ACGTCCTTACCACAAAACACTCCCGTACCTACCTCTTCACGGTTCCCGGG				

1. AB01265	10	20	30	40	50
[ 1790 ]	TCGAGGATCCGGGTACCATGGCTGCATCCCAGCAGCAGCAGCACTTCTCT>				
huFGF-L	TGCAGGAATGGTGTGTTTTGTGAGGGCATGGATGGAGAAGTGCCAAGGGCCC				

	160	170	180	190	200
huFGF-L	CTGTTTGGTCACTTCCGAAGAGCAAAAACGTGTTGAGAGGAGACCGGTTT				
	GACAAACCAGTGAAGGCTTCTCGTTTTTGCACAACTCTCCTCTGGCCAAA				

		T			
1. AB01265	60		70	80	90
[ 1790 ]	GGCTCAAGGCACT-TCTCT-GG-CTCTT-CTGTGGCTCACACAGTGGTGG>				
huFGF-L	CTGTTTGGTCACTTCCGAAGAGCAAAAACGTGTTGAGAGGAGACCGGTTT				

	210	220	230	240	250
huFGF-L	AAGATTTCAAACAGAACCTCCCCAGCGCGCATGAAAGGACTTGATTAGCA				
	TTCTAAAGTTTGTCTTGGAGGGGTCGCGCGTACTTTCCTGAACCTAATCGT				

1. AB01265	110	120	130	140
[ 1790 ]	CTTCTTTTACATGTCATTTGGC-CTCACTC-ACACCTGAGTCTGC-TG-C>			
huFGF-L	AAGATTTCAAACAGAACCTCCCCAGCGCGCATGAAAGGACTTGATTAGCA			

	260	270	280	290	300
huFGF-L	TATGTCAAGAGGACCCGCTTATATACTCGGTGTGTATGTACACAGGACTC ATACAGTTCTCCTGGGCGAATATATAGCCACACATACATGTGTCCTGAG				
1. AB01265	150	160	170	180	190
[ 1790 ]	-TGCTGATGATGATGCCCCCTCTC-TCAATGT-GGATTATGGTGATGACGG>				
huFGF-L	TATGTCAAGAGGACCCGCTTATATACTCGGTGTGTATGTACACAGGACTC				
	310	320	330	340	350
huFGF-L	TGATCTGATCAGTTTGC GGAATTGGAGCCCCAGCCAACAGCCCTAGTCCT ACTAGACTAGTCAAACGCCTTAACCTCGGGGTCGGTTGTCGGGATCAGGA				
	A				T
1. AB01265	200	210	220	230	240
[ 1790 ]	TG-ACTACGCTGCAT-GTGA-ATGGCCCTGCGATGAAAAGAAGCACTTTG>				
huFGF-L	TGATCTGATCAGTTTGC GGAATTGGAGCCCCAGCCAACAGCCCTAGTCCT				
	360	370	380	390	400
huFGF-L	AGTATTGGCAGCGGCAGCTATAGATATTTCTGCAGAGCCAGCAGCCGGCT TCATAACCGTCGCCGTCGATATCTATAAAGACGTCTCGGTCTCGGCCGA				
				GTC	
				CTTT	T
1. AB01265	250	260	270	280	290
[ 1790 ]	CACATCCTTACCAGTGCCTTGGCAGGTGTGAACAGAGAGAGGAAGTGTGCG>				
huFGF-L	AGTATTGGCAGCGGCAGCTATAGATATTTCTGCAGAGCCAGCAGCCGGCT				
	410	420	430	440	450
huFGF-L	CCCACCTACCCAAGGAGAGAAGATCGCTCCAAGACAGTGAGAGCTTCCCT GGGTGGATGGGTTCCCTCTCTTCTAGCGAGGTTCTGTCACTCTCGAAGGGA				
1. AB01265	310	320	330	340	
[ 1790 ]	ACAACGTGCTTCATT-A-ACATA-T-G-TCAACTTGGCC-AATATACATA>				
huFGF-L	CCCACCTACCCAAGGAGAGAAGATCGCTCCAAGACAGTGAGAGCTTCCCT				
	460	470	480	490	500
huFGF-L	GCCATTTCAAGTGCAAAGTCCCTCCGGAGCGACCTCAGAGGAGTAACCGGG CGGTAAAGTCACGTTTCAGGGAGGCCTCGCTGGAGTCTCCTCATTGGCCC				
1. AB01265	350	360	370	380	390
[ 1790 ]	GGCTTCGTACTTATAGCGGCCAGCAGCGCGCACTCA-GCTATTAGCCCAG>				
huFGF-L	GCCATTTCAAGTGCAAAGTCCCTCCGGAGCGACCTCAGAGGAGTAACCGGG				

	510	520	530	540	550
huFGF-L	CCTTAACTTTTTGCGCTCGTTTTGCTATAATTTTTCTCTATCCACCTCCA				
	GGAATTGAAAAACGCGAGCAAAACGATATTAAAAAGAGATAGGTGGAGGT				
1. AB01265	400	410	420	430	440
[ 1790 ]	AGCTCTGGAGAAGGTCACTACATGCCGAACTGATC-TG-AC-CCGGAC->				
huFGF-L	CCTTAACTTTTTGCGCTCGTTTTGCTATAATTTTTCTCTATCCACCTCCA				
	560	570	580	590	600
huFGF-L	TCCCACCCCCACAACACTCTTTACTGGGGGGGTCTTTTGTTGTTCCGGATC				
	AGGGTGGGGGTGTTGTGAGAAATGACCCCCCAGAAAACACAAGGCCTAG				
			GATC	TCACCCG	CA
1. AB01265	450	460		480	500
[ 1790 ]	ACTTGTTTCACCAACGTTCTTTTTTGGTTTGGATTGTGTGCCTTAGATA>				
huFGF-L	TCCCACCCCCACAACACTCTTTACTGGGGGGGTCTTTTGTTGTTCCGGATC				
	610	620	630	640	650
huFGF-L	TCCCCCTCCATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT				
	AGGGGGAGGTACCGAGGGAATCGGCTTCAGCCCCGAAAGACCCGCCGGA				
1. AB01265	510	520	530	540	550
[ 1790 ]	TTGCG-CACATGGCTCCTCTGGCCGACGTGGGCACCTTCCTCGGTGGGTA>				
huFGF-L	TCCCCCTCCATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT				
	660	670	680	690	700
huFGF-L	GGAGGGCTTGGGCCAGCAGGTGGGTTCGCATTTCTGTTGCCTCCTGCCG				
	CCTCCCGAACCCGGTCGTCCACCCAAGCGTAAAGGACAACGGAGGACGGC				
1. AB01265	560	570	580	590	
[ 1790 ]	TGATGCCCTTG---GGCAGGTGGGCTCCCACCTTCTTGCTGCCGCTGCCA>				
huFGF-L	GGAGGGCTTGGGCCAGCAGGTGGGTTCGCATTTCTGTTGCCTCCTGCCG				
	710	720	730	740	750
huFGF-L	GGGAGCGGCCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC				
	CCCTCGCCGGCGGCGACGACCCGCTCGCGTCCTCGCGCCGCCTCGCCTCG				
				C	
1. AB01265	0	610	620	630	640
[ 1790 ]	AGGACAGCCCCCTGCTCTTCAACG-ACCCACTGGCTAGTCGGAGCGACTT>				
huFGF-L	GGGAGCGGCCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC				

		760	770	780	790	800
huFGF-L		GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT CGGGCGCCGCCCGGCCCCCGACGCGTCGACCGCGTGGACGTGCCGTAGGA				
1. AB01265	0	660	670	680	690	
[ 1790 ]	TCCCGCAG--CGC---CCCCTCC-GACCTCTCCCATCTCCAGGGAATCTT> 					
huFGF-L	GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT					
		810	820	830	840	850
huFGF-L	GCGCCGCGGCAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC CGCGGCGGCCGTCGAGATAACGGCGTGGCCGAAGGTGGACGTCTAGGACG					
1. AB01265	700	710	720	730	740	
[ 1790 ]	GCGCCGCGCCAGCTCTATTGTAGGACCGGCTTCCACCTGCAGATACTGC> 					
huFGF-L	GCGCCGCGGCAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC					
		860	870	880	890	900
huFGF-L	CCGACGGCAGCGTGACAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC GGCTGCCGTCGCACGTCCCCGTGGGCCGTCTGGTGTGGGAGAAGCCATAG					
1. AB01265	750	760	770	780	790	
[ 1790 ]	CGGACGGGAACGTGCAGGGCACTCGGCAGGATCACAGCCGATTTCGGTATC> 					
huFGF-L	CCGACGGCAGCGTGACAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC					
		910	920	930	940	950
huFGF-L	TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA AACCTTAAGTAGTCACACCGTCACCCTGACCAGTCATAATCTCCACACCT					
1. AB01265	800	810	820	830	840	
[ 1790 ]	CTAGAATTTATCAGTGTGCTATTGGCCTGGTTAGCATTTCGAGGGGTGGA> 					
huFGF-L	TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA					
		960	970	980	990	1000
huFGF-L	CAGTGGTCTCTATCTTGAATGAATGACAAAGGAGAACTCTATGGATCAG GTCACCAGAGATAGAACCTTACTTACTGTTTCCTCTTGAGATACCTAGTC					
1. AB01265	850	860	870	880	890	
[ 1790 ]	CACCGGCCTTTACCTTGGGATGAATGATAAAGGAGAACTTTTCGGATCGG> 					
huFGF-L	CAGTGGTCTCTATCTTGAATGAATGACAAAGGAGAACTCTATGGATCAG					





	1260	1270	1280	1290	1300
huFGF-L	GATAGTGACATTATGGAAGAGTCAAACCACAACCATTCTTTCTTGTCATA				
	CTATCACTGTAATACCTTCTCAGTTTGGTGTGGTAAGAAAGAACAGTAT				
1. AB01265	1150	1160	1170	1180	1190
[ 1790 ]	GCACCTGG-CCTCTA-GAGGGATGTACAAGAAACCTTGGCTTTTCACAAA>				
huFGF-L	GATAGTGACATTATGGAAGAGTCAAACCACAACCATTCTTTCTTGTCATA				
	GATAGTGACATTATGGAAGAGTCAAACCACAACCATTCTTTCTTGTCATA				
	1310	1320	1330		
huFGF-L	GTTCCCATCATAAAATAATGACCCAAGCAG				
	CAAGGGTAGTATTTTATTACTGGGTTTCGTC				
1. AB01265	1200				
[ 1790 ]	GAAAGG-AG-AGAAACAGT-GC>				
huFGF-L	GTTCCCATCATAAAATAATGAC				

## EXHIBIT G

huFGF-L	10	20	30	40	50
	TACACGGCCGCGAGCTGAACAGCATCACCGCTGTCCCAAGGACAACCCCAA				
	ATGTGCCGCGCTCGACTTGTCTAGTGGCGACAGGGTTCCTGTTGGGGTT				
2. AA232729	10	20	30	40	50
[ 1972 ]	TACACGGCCGCGAGCTGAACAGCATCACCGCTGTCCCAAGGACAACCCCAA>				
huFGF-L	TACACGGCCGCGAGCTGAACAGCATCACCGCTGTCCCAAGGACAACCCCAA				
huFGF-L	60	70	80	90	100
	AGAGGGGCGCTCGACTGCACCTCCTCGAAGTTGCTGGCTGGCTTTGGCAAG				
	TCTCCCCGGAGCTGACGTGGAGGAGCTTCAACGACCGACCGAAACCGTTC				
2. AA232729	60	70	80	90	100
[ 1972 ]	AGAGGGGCGCTCGACTGCACCTCCTCGAAGTTGCTGGCTGGCTTTGGCAAG>				
huFGF-L	AGAGGGGCGCTCGACTGCACCTCCTCGAAGTTGCTGGCTGGCTTTGGCAAG				
huFGF-L	110	120	130	140	150
	TGCAGGAATGGTGTGTTTTGTGAGGGCATGGATGGAGAAGTGCCAAGGGCCC				
	ACGTCTTACCACAAAACACTCCCGTACCTACCTCTTCACGGTTCCCGGG				
2. AA232729	110	120	130	140	150
[ 1972 ]	TGCAGGAATGGTGTGTTTTGTGAGGGCATGGATGGAGAAGTGCCAAGGGCCC>				
huFGF-L	TGCAGGAATGGTGTGTTTTGTGAGGGCATGGATGGAGAAGTGCCAAGGGCCC				
huFGF-L	160	170	180	190	200
	CTGTTTGGTCACTTCCGAAGAGCAAAAACGTGTTGAGAGGAGACCGGTTT				
	GACAAACCAGTGAAGGCTTCTCGTTTTTGCACAACCTCTCCTCTGGCCAAA				
2. AA232729	160	170	180	190	200
[ 1972 ]	CTGTTTGGTCACTTCCGAAGAGCAAAAACGTGTTGAGAGGAGACCGGTTT>				
huFGF-L	CTGTTTGGTCACTTCCGAAGAGCAAAAACGTGTTGAGAGGAGACCGGTTT				
huFGF-L	210	220	230	240	250
	AAGATTTCAAACAGAACCTCCCCAGCGCGCATGAAAGGACTTGATTAGCA				
	TTCTAAAGTTTGTCTTGGAGGGGTCGCGCGTACTTTCCTGAACTAATCGT				
2. AA232729	210	220	230	240	250
[ 1972 ]	AAGATTTCAAACAGAACCTCCCCAGCGCGCATGAAAGGACTTGATTAGCA>				
huFGF-L	AAGATTTCAAACAGAACCTCCCCAGCGCGCATGAAAGGACTTGATTAGCA				

	260	270	280	290	300
huFGF-L	TATGTCAAGAGGACCCGCTTATATACTCGGTGTGTATGTACACAGGACTC				
	ATACAGTTCTCCTGGGCGAATATATGAGCCACACATACATGTGTCCTGAG				
2. AA232729	260	270	280	290	300
[ 1972 ]	TATGTCAAGAGGACCCGCTTATATACTCGGTGTGTATGTACACAGGACTC>				
huFGF-L	TATGTCAAGAGGACCCGCTTATATACTCGGTGTGTATGTACACAGGACTC				
	310	320	330	340	350
huFGF-L	TGATCTGATCAGTTTGC GGAATTGGAGCCCCAGCCAACAGCCCTAGTCCT				
	ACTAGACTAGTCAAACGCCTTAACCTCGGGGTCGGTTGTCGGGATCAGGA				
2. AA232729	310	320	330	340	350
[ 1972 ]	TGATCTGATCAGTTTGC GGAATTGGAGCCCCAGCCAACAGCCCTAGTCCT>				
huFGF-L	TGATCTGATCAGTTTGC GGAATTGGAGCCCCAGCCAACAGCCCTAGTCCT				
	360	370	380	390	400
huFGF-L	AGTATTGGCAGCGGCAGCTATAGATATTTCTGCAGAGCCAGCAGCCGGCT				
	TCATAACCGTCGCCGTCGATATCTATAAAGACGTCTCGGTCGTCGGCCGA				
2. AA232729	360	370	380	390	400
[ 1972 ]	AGTATTGGCAGCGGCACGTATAGATATTTCTGCAGAGCCAGCAGCCGGCT>				
huFGF-L	AGTATTGGCAGCGGCAGCTATAGATATTTCTGCAGAGCCAGCAGCCGGCT				
	410	420	430	440	450
huFGF-L	CCCACCTACCCAAGGAGAGAAGATCGCTCCAAGACAGTGAGAGCTTCCCT				
	GGGTGGATGGGTTCCCTCTCTTCTAGCGAGGTTCTGTCACTCTCGAAGGGA				
2. AA232729	410	420	430	440	450
[ 1972 ]	CCCACCTACCCAAGGAGAGAAGATCGCTCCAAGACAGTGAGAGCTTCCCT>				
huFGF-L	CCCACCTACCCAAGGAGAGAAGATCGCTCCAAGACAGTGAGAGCTTCCCT				
	460	470	480	490	500
huFGF-L	GCCATTTTCAGTGCAAAGTCCCTCCGGAGCGACCTCAGAGGAGTAACCGGG				
	CGGTAAAGTCACGTTTCAGGGAGGCCTCGCTGGAGTCTCCTCATTGGCCC				
2. AA232729	460	470	480	490	
[ 1972 ]	GCCATTTTCAGTGCAAAGTCCCTCCGGAGCGACCTCAGAGGAGTAAC>				
huFGF-L	GCCATTTTCAGTGCAAAGTCCCTCCGGAGCGACCTCAGAGGAGTAAC				
	510	520	530	540	550
huFGF-L	CCTTAACCTTTTTCGCTCGTTTTCGTATAATTTTCTCTATCCACCTCCA				
	GGAATTGAAAAACGCGAGCAAAACGATATTAAGAGATAGGTGGAGGT				

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                    560      570      580      590      600
huFGF-L  TCCCCACCCCAACAACACTCTTTACTGGGGGGGTCTTTTGTGTTCCGGATC
          AGGGTGGGGGTGTTGTGAGAAATGACCCCCCAGAAAACACAAGGCCTAG

                    610      620      630      640      650
huFGF-L  TCCCCCTCCATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT
          AGGGGGAGGTACCGAGGGAATCGGCTTCAGCCCCCGAAAGACCCGCCGGA

1. huFGF-L O      10      20      30      40
[ 2544 ]          ATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT>
                  |||||
huFGF-L          ATGGCTCCCTTAGCCGAAGTCGGGGGCTTTCTGGGCGGCCT

                    660      670      680      690      700
huFGF-L  GGAGGGCTTGGGCCAGCAGGTGGGTTCGCATTTCTGTGCTCCTGCCG
          CCTCCCGAACCCTGTCCTCACCCTAAGCGTAAAGGACAACGGAGGACGGC

1. huFGF-L O      50      60      70      80      90
[ 2544 ]          GGAGGGCTTGGGCCAGCAGGTGGGTTCGCATTTCTGTGCTCCTGCCG>
                  |||||
huFGF-L          GGAGGGCTTGGGCCAGCAGGTGGGTTCGCATTTCTGTGCTCCTGCCG

                    710      720      730      740      750
huFGF-L  GGGAGCGGCCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC
          CCTCGCCGGCGGCGACGACCCGCTCGCGTCCTCGCGCCGCCTCGCCTCG

1. huFGF-L O      100     110     120     130     140
[ 2544 ]          GGGAGCGGCCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC>
                  |||||
huFGF-L          GGGAGCGGCCCGCTGCTGGGCGAGCGCAGGAGCGCGGCGGAGCGGAGC

                    760      770      780      790      800
huFGF-L  GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT
          CGGGCGCCGCCCGGCCCCCGACGCGTCGACCGCGTGGACGTGCCGTAGGA

1. huFGF-L O      150     160     170     180     190
[ 2544 ]          GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT>
                  |||||
huFGF-L          GCCCGCGGCGGGCCGGGGGCTGCGCAGCTGGCGCACCTGCACGGCATCCT

                    810      820      830      840      850
huFGF-L  GCGCCGCGGCGAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC
          CGCGGCGGCCGTGAGATAACGGCGTGGCCGAAGGTGGACGTCTAGGACG

1. huFGF-L O      200     210     220     230     240
[ 2544 ]          GCGCCGCGGCGAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC>
                  |||||
huFGF-L          GCGCCGCGGCGAGCTCTATTGCCGCACCGGCTTCCACCTGCAGATCCTGC

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		860	870	880	890	900
huFGF-L		CCGACGGCAGCGTGCAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC				
		GGCTGCCGTCGCACGTCCCCTGGGCCGTCTGGTGTGGAGAAGCCATAG				
1. huFGF-L	O	250	260	270	280	290
[ 2544 ]		CCGACGGCAGCGTGCAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC>				
huFGF-L		CCGACGGCAGCGTGCAGGGCACCCGGCAGGACCACAGCCTCTTCGGTATC				
		910	920	930	940	950
huFGF-L		TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA				
		AACCTTAAGTAGTCACACCGTCACCCTGACCAGTCATAATCTCCACACCT				
1. huFGF-L	O	300	310	320	330	340
[ 2544 ]		TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA>				
huFGF-L		TTGGAATTCATCAGTGTGGCAGTGGGACTGGTCAGTATTAGAGGTGTGGA				
		960	970	980	990	1000
huFGF-L		CAGTGGTCTCTATCTTTGGAATGAATGACAAAGGAGAACTCTATGGATCAG				
		GTCACCAGAGATAGAACCTTACTTACTGTTTCTCTTGAGATACCTAGTC				
1. huFGF-L	O	350	360	370	380	390
[ 2544 ]		CAGTGGTCTCTATCTTTGGAATGAATGACAAAGGAGAACTCTATGGATCAG>				
huFGF-L		CAGTGGTCTCTATCTTTGGAATGAATGACAAAGGAGAACTCTATGGATCAG				
		1010	1020	1030	1040	1050
huFGF-L		AGAAACTTACTTCCGAATGCATCTTTAGGGAGCAGTTTGAAGAGAACTGG				
		TCTTTGAATGAAGGCTTACGTAGAAATCCCTCGTCAAACCTTCTCTTGACC				
1. huFGF-L	O	400	410	420	430	440
[ 2544 ]		AGAAACTTACTTCCGAATGCATCTTTAGGGAGCAGTTTGAAGAGAACTGG>				
huFGF-L		AGAAACTTACTTCCGAATGCATCTTTAGGGAGCAGTTTGAAGAGAACTGG				
		1060	1070	1080	1090	1100
huFGF-L		TATAACACCTATTCATCTAACATATATAAACATGGAGACACTGGCCGCAG				
		ATATTGTGGATAAGTAGATTGTATATATTTGTACCTCTGTGACCGGCGTC				
1. huFGF-L	O	450	460	470	480	490
[ 2544 ]		TATAACACCTATTCATCTAACATATATAAACATGGAGACACTGGCCGCAG>				
huFGF-L		TATAACACCTATTCATCTAACATATATAAACATGGAGACACTGGCCGCAG				

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          1110      1120      1130      1140      1150
huFGF-L    GTATTTTGTGGCACTTAACAAAGACGGAAGCTCCAAGAGATGGCGCCAGGT
          CATAAAACACCGTGAATTGTTTCTGCCTTGAGGTTCTCTACCGCGGTCCA

1. huFGF-L O      500      510      520      530      540
[ 2544 ]    GTATTTTGTGGCACTTAACAAAGACGGAAGCTCCAAGAGATGGCGCCAGGT>
          |||
huFGF-L    GTATTTTGTGGCACTTAACAAAGACGGAAGCTCCAAGAGATGGCGCCAGGT

          1160      1170      1180      1190      1200
huFGF-L    CCAAGAGGCATCAGAAATTTACACATTTCTTACCTAGACCAGTGGATCCA
          GGTTCCTCCGTAGTCTTTAAATGTGTAAAGAATGGATCTGGTCACCTAGGT

1. huFGF-L O      550      560      570      580      590
[ 2544 ]    CCAAGAGGCATCAGAAATTTACACATTTCTTACCTAGACCAGTGGATCCA>
          |||
huFGF-L    CCAAGAGGCATCAGAAATTTACACATTTCTTACCTAGACCAGTGGATCCA

          1210      1220      1230      1240      1250
huFGF-L    GAAAGAGTTCCAGAATTGTACAAGGACCTACTGATGTACACTTGAAGTGC
          CTTTCTCAAGGTCTTAACATGTTCTCGGATGACTACATGTGAACTTCAG

1. huFGF-L O      600      610      620      630
[ 2544 ]    GAAAGAGTTCCAGAATTGTACAAGGACCTACTGATGTACACTTGA>
          |||
huFGF-L    GAAAGAGTTCCAGAATTGTACAAGGACCTACTGATGTACACTTGA

          1260      1270      1280      1290      1300
huFGF-L    GATAGTGACATTATGGAAGAGTCAAACCACAACCATTCTTTCTTGTCATA
          CTATCACTGTAATACCTTCTCAGTTTGGTGTGGTAAGAAAGAACAGTAT

          1310      1320      1330
huFGF-L    GTTCCCATCATAAAATAATGACCCAAGCAG
          CAAGGGTAGTATTTTATTACTGGGTTTCGTC

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